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EXAMINER

SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 08/23/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/444,388

Applicant(s)

HIBINO ET AL.

Examiner

Jehanne Souaya

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-8 and 10-15 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8 and 10-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Currently, claims 6-8, and 10-15 are pending in the instant application. Claims 6-7 are withdrawn from consideration as being drawn to non elected inventions. Claims 8 and 10-15 are currently under examination. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. This action is NON-FINAL.

The amendment to claim 11, from *Acacia auricaliformis* to *Acacia auriculiformis* is not considered new matter as the recitation of *auricaliformis* in the specification is an obvious error and one of skill in the art would recognize that the correct spelling for such was *auriculiformis* as the species *auricaliformis* was not known in the art at the time of applicant's invention.

MPEP§2163.07 states "An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction. *In re Oda*, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971)."

Continued Prosecution Application

2. The request filed on June 5, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/444,388 is acceptable and a CPA has been established. An action on the CPA follows.

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Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

New Grounds of Rejection and objection

Claim Objections

4. Claim 10 is objected to because of the following informalities: the recitation of *Acaia* appears to be a misspelling. Claim 12 is objected to because the recitation of "representation difference analysis method" is grammatically incorrect. Applicant can overcome the objection to claim 12 by reciting instead "representation difference analysis". Appropriate correction is required.

5. The amendment filed 8/13/2001 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: in claim 8, step d, the recitation of "wherein the primers are designed to hybridize to the mRNA for a plant gene related to the breeding marker". In claim 14, the recitation of "primers *comprise* the sequences of SEQ ID NOS 1 and 2".

Applicant is required to cancel the new matter in the reply to this Office Action.

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Claim Rejections - 35 USC § 112

New Matter and Written Description

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 8 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claim 8 recites the following phrase in step d: “wherein the primers are designed to hybridize to the mRNA for a plant gene related to the breeding marker” (The amendment filed 8/13/2001 added claim 8 with the phrase in quotation above). Such recitation is not supported by the specification and therefore, the specification does not provide adequate description of a cDNA amplified by oligonucleotide primers that are designed to hybridize to the mRNA for a plant gene related to the breeding marker nor a method of using such a cDNA. In the amendment filed 8/13/2001, it is asserted at page 3 that claim 8 finds general support, inter alia, in canceled claim 1, and specific support in Example 1. The examiner has thoroughly reviewed the specification and found no support for the recitation of “wherein the primers are designed to hybridize to the mRNA for a plant gene related to the breeding marker”, in any of the claims as originally filed, in the specification as a whole, or in example 1. Further, the

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specification does not suggest a cDNA “amplified by oligonucleotide primers that are designed to hybridize to the mRNA for a plant gene related to the breeding marker”. In addition, the specification does not define what is meant by “a plant gene *related* to the breeding marker” in that it is unclear whether the plant gene is associated with the breeding marker, linked to the breeding marker, or contains the breeding marker. Such a broad recitation encompasses hundreds of genomic sequences that have not been taught or described in the specification. With regard to specific example 1 in the specification, the example teaches cDNA amplified by SEQ ID NOS 1 and 2, however, the specification does not teach or suggest that such primers “are primers that are designed to hybridize to the mRNA for a plant gene related to the breeding marker”. Furthermore, the specification does not teach or explain how the primers of SEQ ID NO 1 and 2 were constructed, nor does a search of nucleic acid sequence databases such as Genbank reveal what the origin of SEQ ID NOS 1 and 2 are, therefore such would not be obvious to a skilled artisan. It would further not be obvious to one of skill in the art that SEQ ID NOS 1 and 2 were “primers designed to hybridize to the mRNA for a plant gene related to the breeding marker” as neither the art nor the specification teach or suggest such.

Amended claim 14 (amendment filed 8/13/01) recites “primers comprise the sequences of SEQ ID NOS 1 and 2”, however the specification only teaches primers consisting of the sequence of SEQ ID Nos 1 and 2 and does not teach or suggest using primers that ‘comprise’ sequences of SEQ ID NO 2.

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Written Description

8. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 14 is drawn to a general method of claim 8 using primers "comprising the sequences of SEQ ID NOS 1 and 2". The recitation of the word "comprising" thus encompasses sequences with an unspecified number of nucleic acids on either side of SEQ ID NOS 1 and 2. Such recitation encompasses a method that uses oligonucleotide sequences containing undisclosed nucleic acid sequences including genomic DNA and cDNA, that are neither described nor suggested by the specification. The specification does not teach the sequence of the nucleic acid sequence, or a full length open reading frame or gene, that SEQ ID NOS 1 and 2 were constructed from and therefore, the sequences appear to be random. The recitation of the word "comprising" encompasses a large genus of undisclosed nucleic acids that include both wildtype and mutant coding as well as genomic DNA sequences that are neither taught nor described by the specification. With the exception of a sequence "consisting of SEQ ID NO 1 or 2", the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the simplicity of the method of isolation, absent further guidance. Neither the methods nor the teachings described in the specification provide the skilled artisan with any suggestion as to the identity or specific primary structure (that is the nucleic acid

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sequence itself) of sequences "comprising SEQ ID NOS 1 and 2" and thus the disclosed structural feature (SEQ ID NO 1, SEQ ID NO 2) is not representative of the claimed genus.

Applicant should note that because "sequences comprising SEQ ID NOS 1 and 2" do not meet the description requirement, a method of using such sequences also lacks sufficient written description.

Indefinite

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 8 and 10-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 8 is indefinite in the recitation "hybridize to the mRNA for a plant gene *related* to the breeding marker" in step d, as it unclear from the recitation in the claim, nor does the specification define what is encompassed by "related to the breeding marker". For example, it is unclear if the primers designed to hybridize to the mRNA for a plant gene "related" to a breeding marker refers to primers that hybridize to the DNA fragments of step c, if the primers hybridize to any DNA sequence from one of the original sibling plants, or if the primers hybridize to any sequence linked to or associated with the breeding marker. Because the specification does not define the phrase, the metes and bounds of the claim are unclear. Step d is further indefinite because the first part of step d recites that the probe is a labeled cDNA of all

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mRNA obtained from the two individuals and the second part appears to recite that the probe is in fact only a specific set of cDNAs, whose identification is unclear.

B) Claim 8 is indefinite in the recitation of step f as it is unclear if the method of step f involves genome subtraction between the genomic DNA of the same individual or if it involves a genome subtraction between genomic DNA of one of the individuals and the DNA fragments of step c. The claim does not make clear if the former is the case because step f recites “repeating steps c-e” however step c recites “by inter-individual genome subtraction”, thus it is unclear how “inter-individual” can encompass the former.

C) Claim 8 is indefinite as it does not include a positive process step relating back to the preamble. The preamble of claim 8 recites “a method of obtaining a DNA fragment” while the last step of claim 8 is directed to “identifying the DNA fragment” thus it is unclear if the claim is directed to actually “obtaining a fragment” or to simply “identifying a fragment”.

D) Claim 8 is indefinite as it is unclear if the “plant” in section a is a forest tree plant as stated in the preamble or any plant, which encompasses plants other than forest trees.

E) Claim 8 is indefinite as it appears to be missing step g, the method lists a step f and a step h, but no step g, therefore, it is unclear if this is a typographical error, or if there is a missing step in the claim.

F) Claim 11 lacks sufficient antecedent basis for the recitation of “the Acacia” as the term Acacia does not appear previously in the claim or any claim from which claim 11 depends.

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Claim Rejections - 35 USC § 103

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 8, 10-12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips in view of Wigler and Frazer et al (Journal of Immunological methods, vol. 207, p 1-12, 1997) and further in view of Pinyopusarerk.

The claims are drawn to a method for obtaining a DNA fragment for a breeding marker for polymorphic forest tree plants comprising the following steps: a) selecting two sibling individuals of a plant having different phenotypes, b) obtaining genomic DNA from the two individuals, c) selecting DNA fragments by a genome subtraction between the genomic DNA of the two individuals, d) providing a labeled cDNA probe that has been obtained from total mRNA of both individuals [it is noted that because the specification does not define what is encompassed by the term “related” in step d, that the cDNA probe was constructed using primers for mRNA from the individual that the fragments are selected from in step c - that is, that the phrase “primers hybridize to mRNA for a plant gene ‘related’ to the breeding marker” means that the mRNA comes from the individual sibling that the “selected DNA fragments” fragments came from in step c], e) fractionating the DNA fragments obtained by step c with the probe of step d, f) repeating steps c-e with genomic DNA from one of the individuals wherein the genome subtraction is performed between samples of the genomic DNA of only one individual (it is

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noted that step f of claim 8 is unclear - see 112/2nd rejection above- and that the claim is being interpreted by the examiner to be “intra-individual” genome subtraction), and h) [g??, see 112/2nd rejection above] comparing the DNA fragments of steps e and f to exclude the DNA fragments containing intra-individual polymorphisms to identify the DNA fragment related to the breeding marker.

Phillips teaches a subtraction cloning scheme for *Arabidopsis thaliana*, which resulted in the isolation of differentially regulated cDNA (see abstract). The method of Phillips involves isolating total mRNA from plant material (p. 604), followed by subtractive hybridization using excess ‘driver’ poly(A)+ RNA from control treated plants with first strand cDNA from GA treated plants to generate pools of either GA induced or GA repressed sequences (see p. 605, col. 1). Phillips teaches that clones representing mRNA changed in abundance by GA were selected from enriched libraries by differential hybridization (see p. 607, col. 1 “Identification of GA-regulated clones”)[steps a-c of claim 8]. Phillips teaches that the probes for differential hybridization were generated from single stranded cDNA obtained from poly(A)+ mRNA (p. 607, col. 1). Although Phillips does not teach using polyA+ mRNA from both individuals, Phillips does teach obtaining it from one or the GA-treated or control sample, therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used polyA+ (total) mRNA from both samples as such would save time from having to do so with one individual sample at a time [step d of claim 8]. Phillips teaches that the single stranded cDNA remaining after subtraction was converted to double stranded DNA by

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primer extension and amplified by PCR and that agarose gel electrophoresis (fractionating DNA fragments in step e of claim 8) revealed that the size range of PCR products was 100-600 base pairs (p. 608, col 2, first full para). Although Phillips does not teach using acrylamide gel electrophoresis (claim 15) to fractionate DNA fragments, it would have been obvious to one of ordinary skill in the art at the time the invention was made that acrylamide gel electrophoresis and agarose gel electrophoresis were equivalent methods of separating DNA fragments. Phillips teaches that differential hybridization of duplicate dot blots of 600 random clones from the enriched cDNA libraries with labeled probes derived from mRNA from GA-treated and control shoots (screening the DNA fragments with RNA derived probe from step e of claim 8) identified only 3-5% strongly hybridizing clones, demonstrating the successful subtraction of abundant DNA species. Phillips teaches that the technique was used to identify two genes whose corresponding mRNA accumulate 24 h after application of GA3 to plants of the *Arabidopsis thaliana* GA-deficient dwarf mutant *gal* (p. 613, col. 1, "Discussion").

Wigler uses a specific genome subtraction method called RDA to identify DNA sequence differences between very closely related genomes. Wigler teaches that it is useful to be able to detect particular DNA sequences which have a function or affect a function of cells, for use in breeding, for example (see col. 1, .lines 20-23). Wigler teaches methods for representational difference analysis (RDA) between two sources of DNA (see col. 2, lines 28-30). Wigler teaches that the method finds use in a variety of situations, such as in determining the presence or absence of particular DNA sequences, particularly associated with recessive or dominant traits

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(col 2, lines 57-60). Wigler teaches that in such a situation, one can compare two related sources (step a of claim 8) of DNA to determine whether they share the particular sequence, where the sequence can be coding or non coding (col 2, lines 60-64) (encompasses genomic DNA, step b of claim 8). Wigler teaches that the method involves the isolation of DNA, where the DNA can be from any source, including plants (see col. 3, lines 47-51). Wigler teaches that in the first stage, DNA is isolated and digested to produce fragments (col. 3, lines 61-65). Wigler teaches that subtractive and kinetic steps are employed in the next stage, in a single operation of hybridization and amplification, which, after several rounds, produces enrichment of target DNA (col. 4, lines 29-65) (step c of claim 8). Wigler teaches that resulting DNA can be used as probes to identify sites which differ (col.5). Wigler teaches that such analysis can be used to define sequences which are present in one member of a family and not in another (see col. 6, lines 1-15). In example 2, Wigler specifically teaches analysis of DNA from two individuals resulting in the detection of a small number of differences between two nearly identical genomes.

Therefore, given the combined teachings of Wigler and Phillips the ordinary artisan would have learned that it was possible to 1) identify DNA sequences related to specific traits that were present in one genome and not in the genome of another individual using genome subtraction, and more specifically RDA, 2) that this method could be used in plants, and 3) that this method could be used to differentiate DNA from closely related genomes, such as genomes in the same family (Wigler, col. 3, lines 52-60), and 4) that genome subtraction was successfully used to isolate DNA sequences related to a specific condition in plants (teachings of Phillips).

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Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that it was possible to screen related plant individuals, such as siblings, to isolate DNA fragments that were associated with a trait found in one individual and not the other as Wigler teaches that RDA is an efficient and useful method for such situations. The genome subtraction method of Phillips to isolate DNA sequences related to a specific condition in plants would have provided a specific example of a genome subtraction method that was an effective way to isolate DNA sequences of interest (related to a specific condition) in plants. The RDA method of Wigler and the genome subtraction method of Phillips use the same sequence of steps except that the RDA method taught by Wigler uses multiple rounds of enrichment (2-4- see col. 5, lines 30-31) and specifies specific ratios of concentration for driver and tester DNA sequences to ensure the most complete and sufficient enrichment (see col 4, lines 41-59) whereas the genome subtraction of Phillips teaches a single round of enrichment and does not specify ratios of driver and tester sequences. However, it would have been obvious to one of ordinary skill in the art, given the teaching of successful isolation of sequences of interest taught by both Wigler and Phillips, that either method of genomic subtraction (taught by Wigler or Phillips) was effective and that the extra rounds of enrichment and specific ratios of tester and driver sequences taught by Wigler were preferred as Wigler teaches that such provides a more efficient enrichment of DNA sequences of interest. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the genomic subtraction portion of the method of Phillips, that is genomic subtraction and DNA sequence identification,

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with the specific RDA method of Wigler (claim 12), as the RDA method of Wigler would have provided a more complete method of genome subtraction. It would have further been prima facie obvious to one of ordinary skill in the art at the time the invention was made that the method of Phillips and Wigler could be used to isolate sequences related to specific traits in one individual and not in another related individual as Wigler teaches such and further teaches that such is useful in methods of breeding. It would have also been prima facie obvious to one of ordinary skill in the art at the time the invention was made that the method of Phillips could be carried out using genomic DNA as Wigler teaches that either coding or non coding DNA can be used, and that any sequence may be used such that it will be inherited in association with DNA sequences associated with the trait (see col. 2, lines 62-64).

It is noted that Phillips and Wigler do not teach a control step that includes an intra-individual subtraction step, however Frazer et al teach that control for RDA experiments are important due to the many manipulations of templates where cross contamination can occur and further teaches that the simplest case involves a tester being subtracted against a driver generated from identical material in order to ascertain the degree to which RDA is able to effectively deplete all sequences common to both pools (see p. 8, col. 2, lines 1-11). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Phillips and Wigler by adding a control step as taught by Frazer because Frazer teaches that such control experiments are needed for RDA experiments. The

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ordinary artisan would have been motivated to use the intra individual genome subtraction taught by Frazer because Frazer teaches that it is the simplest control step.

Although Phillips does not teach a plant that is a forest tree and specifically acacia auriculiformis (claims 10 and 11), Pinyopusarerk teaches that the Royal Forest Department of Thailand revised the species of acacia auriculiformis to be used in its reforestation program and that subsequently tree improvement programs have been planned for the species (see p. 147, col. 1). Pinyopusarerk teaches that the improvement program was started with some specific objectives including 1) improve qualities of the species (eg. stem form) through selection and breeding and 2) produce genetically improved seed and other plant material for plantation establishment. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to identify a breeding marker for ie: stem form for acacia auriculiformis, using the methods taught by Phillips in view of Wigler and Frazer as Phillips teaches the successful identification of genes with a specific phenotype. The ordinary artisan would have been motivated to use the method of Phillips to identify a breeding marker for stem form for acacia auriculiformis as Pinyopusarerk teaches a need for improving the quality of the species.

Response to Arguments

Applicants response traversed the previous rejections made under 35 USC 103.

Applicant's arguments will be addressed on issues not pertaining to the amendment of the claims. The response traverses that Phillips overall method cannot be considered to fall within

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the same field of art as the method of claim 8. This argument was thoroughly reviewed but was not found persuasive. In response to applicant's argument that the teachings of Phillips is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the method of Phillips is in the same field of applicant's endeavor, that is, using genome subtraction to isolate DNA sequences associated with a specific condition in one plant that is not present in another plant. The method of genome subtraction can be used for a number of different applications, as taught by Wigler, such as for breeding in cases when DNA associated with a particular trait is sought. The main criteria for genome subtraction is that two samples have a DNA sequence that is different, in which case genome subtraction can be used to isolate the sequence that is not the same in the two samples. The samples can be from related individuals (as taught by Wigler). In response to applicants assertion that it is unapparent why the examiner considers the reference of Wigler as rectifying Phillips deficiencies, such has been outlined in the rejection above.

13. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips in view of Wigler and Frazer et al (Journal of Immunological methods, vol. 207, p 1-12, 1997) and further in view of Pinyopusarerk as applied to claims 8, 10-12 and 15 above, and further in view of Nainan et al.

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The teachings of Phillips in view of Wigler and Frazer and Pinyopusarerk are outlined above. Although Phillips in view of Wigler and Frazer and Pinyopusarerk do not teach using labeled cDNA labeled with digoxigenin, Nainan teaches a simple system to detect PCR products that has the sensitivity and specificity of nested PCR primer PCR which involves digoxigenin labeled PCR products which can be identified with antidigoxigenin antibodies. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to label the cDNA of the method of Phillips with digoxigenin for the purposes of specifically detecting the cDNA. The ordinary artisan would have been motivated to label the cDNA taught by Phillips with digoxigenin as Nainan teaches that it provides sensitivity and specificity.

Conclusion

14. No claims are allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

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Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Jehanne Souaya
Patent examiner
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August 22, 2002